Co-Administration of GSK 19A04 Adjuvanted Cervical Cancer Vaccine with Combined dTpa-IPV Vaccine in Girls Aged 10—18 Years

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Background: *Cervarix*™ (GlaxoSmithKline), AS04 adjuvanted cervical cancer vaccine, has been shown to be safe, immunogenic and highly effective for the prevention of persistent human papillomavirus (HPV)-16/18 infection and associated precancerous lesions in girls and women aged 15—25 years. Since many countries recommend HPV vaccination in adolescents when other pediatric and adolescent vaccines are routinely administered, co-administration of *Cervarix*™ with other vaccines will be convenient for physicians and vaccinees. This study (108464/NCT00426361) evaluated the immunogenicity and safety of *Cervarix*™ co-administered with *Boostrix*™ Polio (dTpa-IPV, GlaxoSmithKline) a diphtheria-tetanus-acellular pertussis-inactivated polio vaccine. *Methods:* Healthy girls aged 10—18 years were randomized in 3 groups to receive either HPV-16/18 vaccine alone (HPV-16/18 group; $n = 248$), HPV-16/18 co-administered with dTpa-IPV (HPV-16/18+dTpa-IPV group; $n = 252$), or dTpa-IPV vaccine alone ($n = 251$). Immunogenicity (ATP) and safety were assessed 1 month after the first vaccine dose.

Results: Interim data on immunogenicity and safety 1 month after the first dose are presented. Co-administration of HPV-16/18 and dTpa-IPV was demonstrated non-inferior to separate administration of dTpa-IPV, with seroprotection rates of 99.6% for anti-diphtheria and 100% for anti-tetanus antibodies in both groups. Seropositivity rates for anti-pertussis and seroprotection rates for anti-poliovirus type antibodies were $\geq$98.7% and 100%, respectively, in the HPV-16/18+dTpa-IPV group and $\geq$96.5% and $\geq$99.6% in the dTpa-IPV group. Seroconversion rates for anti-HPV 16 and 18 antibodies in initially seronegative subjects were 100% in the HPV-16/18 group and 99.1% in the HPV-16/18+dTpa-IPV group. Post-vaccination GMTs in HPV-16/18+dTpa-IPV group were similarly high as for respective antigens in the HPV-16/18 and dTpa-IPV groups. Co-administration of the two vaccines was generally well-tolerated. No subjects withdrew due to adverse events and no vaccine-related serious adverse events were reported.

Conclusion: Results from this interim analysis show that the co-administration of *Cervarix*™ with *Boostrix*™ Polio

doi:10.1016/j.ijid.2008.05.372

19.027

Preclinical Evaluation of Safety and Immunogenicity of a Novel ALA Auxotropic Bivalent (O1 and O139) Oral Cholera Vaccine Candidates

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Cholera is a diarrheal disease caused by toxigenic *Vibrio cholerae* belonging to O1 and O139 serogroups. Cholera epidemics can be prevented in the future if there is a common vaccine which gives protection for both the serogroups, O1 and O139. However currently available vaccine gives protection only for O1 and do not cross protect cholera caused by O139. Hence, this study was focused to develop a bivalent (O1 and O139) ALA auxotropic vaccine candidates. Using genetic engineering techniques we have developed ALA auxotrophs of O139 and O1 *V. cholerae* by mutating the *hem*A gene and were named VCUSM2 and VCUSM4 respectively. The live bivalent formulation of VCUSM2 and VCUSM4 was tested in animal models for colonization ability, reactogenicity, immunogenicity and protection. Infant mouse colonization assay showed that the bivalent vaccine candidates colonized well but the colonization ability was 1 log lower than the parent wild type strains. Reactogenicity of bivalent vaccine candidates were studied using rabbit ileal loop assay and showed reduced fluid accumulation when compared to the respective wild type strains. When ileal loop assay was carried out in the immunized animals with 10^5 CFU of WT O1 and O139 strains no fluid accumulation was seen, indicating that the bivalent vaccine candidate elicited cholera toxin (CT) neutralizing antibodies. However the unimmunized animals showed marked fluid accumulation at the same concentration. This was further substantiated by the presence of high titer of vibriocidal antibodies (500—1000 fold), anti CT antibodies (5—20 fold) and anti LPS (O1 and O139) antibodies after 4 weeks of immunization. Bivalent vaccine provided 100% protection in RITARD model when challenged with either O1 or O139 virulent wild types *V. cholerae*. These results demonstrated that the bivalent vaccine is highly immunogenic with minimal reactogenicity at high CFU and provides protection against O1 and O139 serogroups of *V. cholerae*.

doi:10.1016/j.ijid.2008.05.373